Understanding and modeling the disintegration of food in the gastrointestinal tract and its consequences on human health

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INRA Agrocampus Ouest – Milk and Egg Science & Technology
Rennes FRANCE
Milk & Egg Science & Technology

Our disciplinary skills
Biochemistry
Microbiology
Molecular biology
Process & technology

In situ systems

Our facilities
Mass spectrometry
Confocal microscopy
Quantitative PCR
Isothermal calorimetry
Technology platform
Biological Resource Centre

75 permanent staffs
135 people in total
Understanding the disintegration of food in the GI tract

Link between food and human health = top research priority

It is also a consumer demand

After ingestion, food are broken down in the gut during digestion, delivering nutrients and biological signals to the body

👉 It is of crucial importance to understand how food are disintegrated in the GI tract and to identify the bioactive molecules released during digestion

Understanding the effect of food on human health
Understanding the disintegration of food in the GI tract

To understand the mechanisms of breakdown of food matrices and their constituents in the gut and identify the beneficial/deleterious food components released.

To determine the impact of the structure of food matrices on these mechanisms.

To model these phenomena in order to develop a reverse engineering approach.

Bioactivities
- Bioactive peptides
- Allergens
- Fatty acids

Gut Immune System
Caseins and whey proteins are:

- Structurally opposite (globular/flexible)
- Differently metabolized (fast/slow proteins)
- Highly digestible (>95%)
- Excellent sources of essential amino acids
Infant formula

- Only alternative to the newborn when breast-feeding is not possible
- A key food at a key stage of human life
  - Only stage of life where milk is the only food in the human diet
  - Nutritional imprinting (effect of the newborn diet on the pathologies he will develop later)
- Efforts have been made in order to mimic human milk composition
  - CN/WP = 40/60
  - Up to 50 ingredients are added
- Difficult (impossible?) to study IF digestion in the newborn for ethical reasons
- Needs relevant *in vitro* and animal models
- Study of the IF protein kinetics of digestion in the piglet
In vivo digestion using the piglet as model

Proteins Lipids Sugars Minerals Eau

Heat treatment + concentration + homogenization + Spray-drying

Formula

Effluent Characterization

Automatic feeding system
28 days

Rehydration

Collaboration I. Luron
INRA St Gilles
Multi-scale characterization of digested infant formula

Proteins  Lipids

Stomach  Duodenum  Jejunum  Ileum

Caseins are rapidly hydrolyzed in the stomach but generate peptides resistant to digestion

Viscosity of the bolus

Macroscopic scale

Molecular scale - ELISA
Peptides identified in vivo

Jejunum at 30 min

β-CN

α_{51}-CN

β-Ig

α-la

Jejunum at 90 min

β-CN

α_{51}-CN

α_{52}-CN

κ-CN

β-Ig

Jejunum at 210 min

β-CN

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Current research

- Digestion of infant formula with more sophisticated models

**Digestion of human milk**

- Dynamic Model
  - pH regulation
  - Dynamic flow
  - [Enzymes] regulation

**Proteomic characterization of effluents**
Understanding and modelling the hydrolysis of milk proteins according to the structure of the dairy matrix

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S LE FEUNTEUN, INRA Grignon
C GAUDICHON, AgroParisTech Paris
B LAROCHE, CNRS Gif-sur-Yvette
Context

- Kinetics of aa bioavailability can be critical for some specific populations: athletes, elderly need fast aa bioavailability.

- β-lactoglobulin is a milk protein rich in leucine and has been shown to restore muscle protein metabolism after food intake in elderly people suffering from sarcopenia (Rieu et al. 2006, 2007).

- β-lactoglobulin is rarely consumed as a purified protein but mostly in processed foods.

- Possible to manufacture dairy products with different microstructures but similar composition.

Does the microstructure of dairy products affect the kinetics of protein digestion and aa bioavailability?
Strategy

Manufacture of an « ultra-low-heat » milk powder

Processing (heat-treatment, gelation…)
→ 6 matrices

Multi-scale characterization of the structure
(rheology, microscopy…)

In vivo digestion in 6 mini-pigs (effluents collected during 7h)

Identification of protein digestion products in the duodenum, jejunum and plasma
(SDS-PAGE, LC-MS-MS, molecular immunology…)

Modelling of the kinetics of hydrolysis of β-Lg and β-CN according to the food microstructure

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The 6 matrices

Ultra-low-heat powder → Raw liquid milk → Heat-treated liquid milk (90°C/10 min) → Rennet gel → Acid gel (3% GDL) → Stirred Acid gel → Rennet gel

Addition of non-absorbable markers to the Mean Residence Time (MRT) in the stomach (gastric emptying)
**In vivo trial**

6 female Göttingen mini-pigs (around 30kg)

Collaboration D. Remond
INRA Theix

2 canulas: *
* end of stomach
* mid-jejunum

† sampling of digestive contents

1 catheter (abdominal aorta)
‡ blood sampling

648 samples collected and analyzed
Analyses

Multi-scale characterization of dairy matrices

- Rheology
- Optical and confocal microscopy
- Granulometry
- SDS-PAGE, ELISA

Digestive effluents characterization
- Nitrogen content
- Ytterbium and chrome quantification by atomic absorption
- Protein characterization (SDS-PAGE, ELISA)
- Peptides characterization (LC-MS-MS)

Plasma characterization
- Amino acid analysis by ion-exchange chromatography
- Peptidome characterization by LC-MS-MS

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Evolution of the $\beta$-lg concentration along the GI tract

The structure of food affects the bioavailability of nutrients
Improving health properties of food by sharing our knowledge on the digestive process

COST Action FA1005
INFOGEST

Chair: Dr. Didier DUPONT, Senior Scientist, INRA, France
**Scientific context and objectives**

Diet-related diseases + age EU population ↑

→ Prevent these pathologies rather than cure them

Gut = interface between food and human body

Digestion releases beneficial food components

**Need to increase our knowledge on the effect of food on human health by increasing our knowledge on food digestion**

**FA1005 objectives**

- Spread and improve current basic knowledge on food digestion
- Identify the beneficial food components released in the gut during digestion
- Support the effect of beneficial food components on human health
- Promote harmonization of currently used digestion models
Working groups

INFOGEST

Dairy
Fruits & Vegetables
Egg

Chair
Didier Dupont - France

Vice-chair
Alan Mackie - UK

Relationship between food structure and nutrient bioaccessibility - bioavailability
WG1

In vitro, in vivo and in silico models of mammalian gastrointestinal digestion
WG2

Evaluation of the health effects
WG3

F Capozzi
Italy

B. De Meulenaer
Belgium

A. Brodkorb
Ireland

I. Recio
Spain

Tor Lea
Norway

A. Bordoni
Italy

BFC identification
Stability during processing
Food multi-scale characterization

Digestion models harmonization
Comparison in vitro / in vivo
Digestion products identification
BFC absorption /bioavailability

Immunomodulatory properties
Regulation of appetite and satiety
Effect of BFC on human microbiota

April 2011 – March 2015
140 scientists - 44 institutions – 23 countries
A strong industrial support

30 companies (large groups and SMEs) from all over Europe
Future events

- 2\textsuperscript{nd} Workshop in Le Croisic (France) on 19-21 October 2011

- 1\textsuperscript{st} International Conference on Food Digestion (+Annual Industry Workshop) in Cesena (Italy) on 19-21 March 2012